420 Rec'd PCT/PTO 20 DEC 1999

FORM PTO-1390 (REV 1-98) U S DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: 0/97286 US

U S APPLICATION NO (If known, see 37 CFR 1 5): 09/446416

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/EP98/03712	16-JUN-1998	20-JUN-1997

TITLE OF INVENTION: PRELOADED IMPLANTATION DEVICE

418 Rec'd PCT/PTO 20 DEC 1999

APPLICANT(S) FOR DO/EO/US: DEHAAN, Pieter and BOS, Thomas J.

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.
3. [ ] This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. [X] A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [ ] is transmitted herewith (required only if not transmitted by the International Bureau).
   b. [X] has been transmitted by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [ ] A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. [X] Amendments to the claims of the International Aplication under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [ ] are transmitted herewith (required only if not transmitted by the International Bureau).
   b. [ ] have been transmitted by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [XX] have not been made and will not be made.
8. [ ] A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).
9. [XX] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. [ ] A translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern document(s) or information included:

11. [X] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. [X] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [X] A FIRST preliminary amendment.
    [ ] A SECOND or SUBSEQUENT preliminary amendment.
14. [ ] A substitute specification.
15. [ ] A change of power of attorney and/or address letter.
16. [ ] Other items or information:

EXPRESS MAIL EL358032570 US

U.S. APPLICATION NO (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO	ATTORNEY'S DOCKET NUMBER
09/446416	PCT/EP98/03712	0/97286 US

17. [X] The following fees are submitted:

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):	CALCULATIONS PTO USE ONLY
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO $1070.00	
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO $930.00	
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO $790.00	
International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) $720.00	
International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) $98.00	
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 840.00
Surcharge of $130.00 for furnishing the oath or declaration later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	
Total claims	6 - 20 =		x $22.00	$
Independent claims	2 - 3 =		x $82.00	$
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ $270.00	$

TOTAL OF ABOVE CALCULATIONS =	$ 840.00
Reduction of 1/2 for filing by small entity, if applicable. A Small Entity Statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28). +	$
SUBTOTAL =	$
Processing fee of $130.00 for furnishing the English translation later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(f)).	$
TOTAL NATIONAL FEE =	$ 840.00
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). $40.00 per property +	$ 40.00
TOTAL FEES ENCLOSED =	$ 880.00
Amount to be refunded:	$
charged:	$ 880.00

a. [ ] A check in the amount of $ _____ to cover the above fees is enclosed.

b. [X] Please charge my Deposit Account No. 02-2334 in the amount of $ 880.00 to cover the above fees. A duplicate copy of this sheet is enclosed.

c. [ ] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. _____. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Gregory R. Muir
AKZO NOBEL PATENT DEPARTMENT
1300 Piccard Drive, Suite 206
Rockville, MD 20850

Gregory R. Muir
SIGNATURE

Gregory R. Muir
NAME

35,293
REGISTRATION NUMBER

EXPRESS MAIL EL358032570US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of:

DE HAAN, Pieter and BOS, Thomas J.

Serial Number: To be assigned Group Art Unit: To be assigned

Filed: Concurrently herewith Examiner: To be assigned

For: PRELOADED IMPLANTATION DEVICE

Corresponding to: PCT/EP98/03612, filed June 16, 1998

PRELIMINARY AMENDMENT

Assistant Commissioner of Patents
Washington, D.C. 20231

December 20, 1999

Sir:

Prior to the calculation of the fee in the above-identified application, please make the following amendments:

IN THE SPECIFICATION:

Page 1, above line 5, please insert the heading -- Background of the Invention: --

Page 4, above line 10, please insert the heading -- Summary of the Invention: --

Page 5, above line 11, please insert the following:

-- Brief Description of the Drawings

Fig. 1 is an illustration of the device in the closed-off position;

Fig. 2 is an illustration of the device in an opened position to allow entry of the implant; and

Fig. 3 shows the implant being pushed toward the tip of the device.

Brief Description of the Preferred Embodiment --

IN THE CLAIMS:

Please amend the claims as follows.

3. (amended) An implantation device according to claim 1, [or 2, characterized by being loaded with] further comprising an implant (8) held in the chamber (7).

Please add the following new claims 4 - 6

-- 4. An implantation device according to claim 3, wherein said implant is a hormonal implant. --

-- 5. An implantation device according to claim 2, further comprising an implant (8) held in the chamber (7).

-- 6. An implantation device according to claim 5, wherein said implant is a hormonal implant. --

REMARKS

Claim 3 is amended and 4 - 6 are added, hereby.

Claims 1 - 6 are presented for examination. It is believed that claims 1 - 6 recite a patentable improvement in the art.

If any additional fees are required with this paper, please charge our Deposit Account No. 02-2334.

Respectfully submitted,

Gregory R. Muir
Attorney for Applicants
Registration No. 35,293

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D9DEHAAN-PRELIMINARY

EXPRESSS MAIL EL358032570US

PRELOADED IMPLANTATION DEVICE

The invention pertains to a pre-loadable implantation device comprising a hollow needle and a body adjoining the needle, the body comprising an elongated part extending along the same axis as the needle, a plunger that can be displaced within the elongated part and the needle, the periphery of the plunger defining a channel in the elongated part, and a chamber capable of holding an implant. The invention also pertains to an implantation device that has actually been preloaded with an implant.

Implantation devices are known and serve to introduce a medicinal implant (small rod, pill, tablet, granule and the like which incorporates a pharmaceutically active substance) subcutaneously into humans or animals, or into subcutaneous tissue of humans or animals in an easy, effective and aseptic way.

The implanting of a pharmaceutical preparation subcutaneously or in subcutaneous tissue is normally used in human and veterinary medicine to achieve, e.g., prolonged action of the pharmacon. The implant introduced (small rod, pill, tablet, granule, etc.) slowly dissolves in the surrounding tissue or slowly releases the pharmacon thereto, and the pharmacon goes into circulation via the blood or the lymph in order then to be transported to the site or sites where it can perform its action. Thus, for example, in gynaecology a tablet containing an oestrogen, for example oestradiol, is implanted in women after double ovariectomy or in women during menopause in order to counteract or prevent certain symptoms from which these women suffer or may suffer. Such oestradiol, or other gynaecological implants are generally inserted subcutaneously into an area where there is relatively little movement, such as the upper outer quadrant of the buttock or the lower abdominal wall. In animals implants which contain hormones are, for example, introduced subcutaneously in order to regulate oestrus.

The invention, as noted above, is in the field of preloadable implantation devices. The term "preloadable" indicates that the device allows the implant to be present within the device before such device is used, i.e. by comprising a chamber capable of holding an implant. Such a chamber, which may have any shape suitable for any desired implant to fit into it, when provided beforehand with the implant (i.e. in the preloaded state) makes it easier to control the desired sterility. Particularly, the invention thus provides easy handling by a specialist or a general practitioner, as well as an easy administration *per se* of the implant: this can be done by simply pushing forward the plunger so as to displace it into the needle and thus insert the implant through the needle into the body.

Preloadable implantation devices of the aforementioned type are known. Thus, e.g. US 5,520,660 discloses a device for administering implants, which comprises an active substance container with injection cannula and plunger. The plunger is arranged in a plunger channel which merges into the lumen of the cannula. A holder-device for the implant is arranged at the lumen-end side of the plunger channel.

Another background art reference on preloaded implantation devices is EP 402 955, which discloses a syringe containing a capsule chamber, a hollow needle (removably) mounted at the front end of the capsule chamber, and a plunger, all mounted on a common axis so that the plunger can be passed through the capsule chamber and into the hollow needle to expel a capsule of a solid preparation from the chamber through the needle into a patients body.

Other disclosures on preloaded implantation devices having, positioned in line, a hollow needle, an implant-containing chamber and a plunger by means of which the implant can be pushed through the needle, include US 4,661,103, US 4,601,699, GB 2-138-298, EP 551 699, and FR 2,231,355.

The present invention provides an implantation device with which not only the above problems are solved, but which also avoids the drawbacks of more old-fashioned methods of subcutaneously introducing tablets containing an active substance. A known implantation device serving this purpose, has bene described in EP 564 038. A major drawback of the above preloadable implantation devices is that they do not enjoy the benefits associated with the implantation device according to EP 564 038.

To have these benefits, it must be possible for the needle to be chamfered at the distal end (tip), specifically in such a way that there is a sharp point with which the skin can be pierced, and is firmly joined at the proximal end to the body. The plunger too (also referred to as a mandrel) has a distal end (tip) which is chamfered, specifically at precisely the same angle as the hollow needle. Thus the plunger can be pushed into the hollow needle in such a way that the chamfered end precisely coincides with the chamfered end of the hollow needle, as a result of which a solid needle is, as it were, produced. With the solid needle formed in this way, the skin and the subcutaneous tissue is pricked at the site where it is desired to introduce the implant, normally at an oblique angle. The advantage of using a chamfered solid needle is that the tissue is split and not punched. As a result, the tissue is damaged to a lesser extent and the healing of the prick proceeds more quickly, virtually without leaving any scar. With a hollow chamfered needle, there is a greater possibility in that some tissue will enter the needle as a result of the punching action, the tissue damage therefore becomes somewhat greater and the healing of the prick lasts somewhat longer, with a greater probability of some visible scar.

The above-described preloadable implantation devices cannot be made to have such a provision. For, the plunger essentially must be in the pushed forward position (so as to enable the chamfered plunger tip to blend with the chamfered needle tip) when a patient is pierced with the needle. In the prior art devices this cannot be done without untimely displacing the implant from the chamber to outside the needle tip.

In EP 564 038, a way of operation has been disclosed which involves placing the implant into a chamber during use of the device, e.g. in a rather precise operation using tweezers. Other disclosures on implantation devices that require loading of the implant during operation include US 1,789,766, US 3,921,632 and DE 806 702. None of these known devices has a chamber capable of holding the implant. This also holds for other known injection devices which have specially designed needle-tips for which, by way of background, reference is made to US 2,751,907 and GB 2,199,247.

As will be clear from the above, with the present invention it is sought to provide an implantation device which can be preloaded, thus making it possible to avoid the step of loading the device with the implant during use, but at the same time has the possibility of being provided with provisions that require the free displaceability of the plunger, such as a plunger which blends with the tip o f the needle, so as to avoid undue damage to the patient's tissue.

This object is fulfilled by the invention. To this end, the invention consists therein, that in an implantation device of the above-identified, preloadable type, the chamber is positioned radially outside the channel and has a directly or indirectly open connection to the channel, the plunger being capable of closing off and opening up the chamber by being displaced.

Although benefits of the present invention can be enjoyed in the case of implantation devices that neither have a chamfered needle tip, nor a chamfered plunger tip, it will be clear that it is preferred according to the invention to have such provisions. In that respect, the invention provides a particular improvement on implantation devices such as described in EP 564 038, US 3,921,632. Essentially, this is the type of devices which comprises a hollow needle with a chamfered tip profile and a body adjoining the needle part, the body comprising (a) an elongated part extending along the same axis as the needle, (b) a plunger that can be displaced within the elongated part and the needle, the plunger having a chamfered tip profile

capable of blending with the needle tip profile, wherein the periphery of the plunger defines a channel in the elongated part, and (c) a chamber capable of holding an implant. The chamber of these known devices not being preloadable, the present invention solves the problem of how to provide a preloadable device without losing the strong benefit of the chamfered plunger profile. As outlined above, the means to solve this problem is that the device is provided with a chamber that is positioned radially outside the channel and has a directly or indirectly open connection to the channel, whereby the plunger is capable of closing off and opening up the chamber by being displaced.

The closing off an opening up of the chamber can be by simple displacement of the plunger. I.e., the chamber has an opening of such dimensions at the side of the plunger that, when the plunger is pulled back to behind the chamber (i.e. is pulled to the rear end of the device, by which is meant the end facing away from the needle), an implant contained within the chamber will automatically fall into the plunger channel. It is also possible to make use of other forces than that of gravity, e.g. by providing the chamber, at the side facing away from the channel, with an elastic means such as a spring, which pushes the implant against the plunger when the chamber is closed off, and which makes the implant be pushed from the chamber into the channel when the plunger has been pulled back. Other means for the closing off of the chamber than just the plunger can be provided. Thus, other possibilities include a chamber closed off by an additional closing means, such as a door which automatically opens upon full withdrawal of the plunger, or any suitable mechanical, electronic or optical means steering the opening up of the chamber so that an implant contained therein can be displaced into the channel on or after the moment that the required space therein has become available by withdrawal of the plunger.

The requirement of the plunger being capable of closing off and opening up the chamber by being displaced not only refers to the way the open connection between the chamber and the channel has been made, it also refers to the longitudinal position of the chamber and the length of the plunger. It will be clear to the person

of ordinary skill in the art, that the plunger should be long enough to be pulled back to behind the chamber, and that it is preferred for the chamber to be at a sufficiently large distance from the rear end of the device so as to allow the plunger to be pulled back sufficiently and still be contained within the body of the device.

The device may contain suitable means to ensure that when the plunger is pushed fully into the needle, the chamfered needle point and the chamfered end of the mandrel coincide precisely. Possible means for providing this include a plunger end (i.e. at the side facing away from the needle) of in itself conventional type, which has a larger diameter than the plunger channel, and thus will prevent the plunger from being pushed forward any further than to the point at which said plunger end bumps against the plunger channel. Other means include a protrusion on the plunger and corresponding insertion in the wall of the plunger channel, *or vice-versa*, designed at such a position that when the plunger has been pushed forward to the desired distance, the protrusion will be fixed into the insertion (comparable to a principle known from an unrelated art, viz. that of well-known ball-points of the BIC® type).

As mentioned above, the chamber has a position radially outside the channel. In general, this means that the chamber has a position which, when the device is being used to administer an implant, can be described as being "above" the channel. By virtue of the direct or indirect open connection of the chamber to the channel, an implant contained within the chamber will actually fall into the channel (as a result of the action of gravity) when the plunger has been withdrawn (pulled backwards) so as to free the part of the channel directly underneath the chamber. Other embodiments, though, are not to be excluded, e.g. a chamber which has a position which, upon use of the device, can be described as being "underneath" the channel and which comprises a spring or the like which may forward an implant into the channel.

In the case of a needle having the, most preferable, chamfered tip and associated chamfered plunger, the device is asymmetric in respect of a virtual central axis. Thus a "bottom" and a "top" side of the device can be defined. In respect thereof, a preferred embodiment is as follows. Considering that the point of the chamfered needle, and consequently also the point of the chamfered plunger, preferably are situated at the bottom side, it is preferred for the chamber capable of holding the implant to be situated at the top side.

The component parts of the device according to the invention and the feeding of a preloaded implant is further explained hereinafter with reference to the schematic drawings.

The figures each depict, in longitudinal cross-section, a device according to the invention. The reference signs in each of the figures having the same meaning, all of the figures display an implantation device (1) having a hollow needle (2) and a body (3) adjoining the needle (2) the body comprising an elongated part (4) extending along the same axis as the needle (2), a plunger (5) that can be displaced within the elongated part (4) and the needle (2), the periphery of the plunger defining a channel (6) in the elongated part (4), and a chamber (7) capable of holding an implant (8).

In FIG.1 a device (1) is shown in which the chamber (7) containing the implant (8) is in the closed-off position. FIG.2 shows a device (1) in which the chamber (7) has been opened up by pulling back the plunger (5) and the implant (8) has been fed into the channel (6). FIG.3 is incorporated to show the further operation of the device (1), viz. the pushing forward of the implant (8) by means of the plunger (5).

The components of the device are generally made of a hard material, for example stainless steel. Certain parts of the device may also be made of a suitable plastic, for example a hard type of PVC, certain nylons, PTFE, acrylates such as PPMA, polypropene, polystyrene, polycarbonate or polyoxymethylene. Preferred synthetic

materials are those that are sterilisable, more particularly those that may withstand γ-sterilisation. Such materials are known to the person of ordinary skill in the art. Preferred synthetic materials are ABS (terpolymer of acrylonitrile, butadiene, and styrene) and SAN (copolymer of styrene and acrylonitrile). Without excluding the possibilities of using other than conventional materials for the needle part and said elongated part, or at least the distal parts thereof, these are generally made of metal, preferably stainless steel. The implantation devices of the invention can be manufactured using conventional techniques known to the person skilled in the art.

The body, which may serve as a handle part or may comprise an additional handle part, is thicker than the needle part and may be tubular, but it may also have a different cross section. The handle part should, of course, have a shape such that the device can easily be handled for the purpose for which the device is intended. Thus, recesses can be provided in which the fingers, for example thumb and index finger, fit in order to enable the device to be held firmly during use.

The implants to be contained within the chamber, and, consequently, the chamber itself, may have any shape. A frequently occurring shape is that of a rod of cylindrical or rectangular cross-section, such as in the case of an implantation tablet which contains oestradiol and which is made under the brand name Dimenformon by N.V. Organon Oss, The Netherlands. Other examples of implants that can be employed to make preloaded implantation devices according to the invention are oestradiol implants such as Riselle®, Meno-Implant®, contraceptive implants such as Implanon®, or other hormonal implants such as testosterone implants. The device of the present invention, besides being suitable for introducing hormonal implants can also be employed for implants containing other active substances than hormones, and can be employed for implantation in other types of tissue beyond lipid tissue.

Claims:

1. An implantation device (1) comprising a hollow needle (2) and a body (3) adjoining the needle, the body (3) comprising an elongated part (4) extending along the same axis as the needle (2), a plunger (5) that can be displaced within the elongated part (4) and the needle (2), the periphery of the plunger (5) defining a channel (6) in the elongated part (4), and a chamber (7) capable of holding an implant (8), characterized in that the chamber (7) is positioned radially outside the channel (6) and has a directly or indirectly open connection to the channel (6), the plunger (5) being capable of closing off and opening up the chamber (7) by being displaced.

2. An implantation device (1) comprising a hollow needle (2) having a chamfered tip profile and a body (3) adjoining the needle (2), the body (3) comprising an elongated part (4) extending along the same axis as the needle (2), a plunger (5) that can be displaced within the elongated part (4) and the needle (2), the plunger (5) having a chamfered tip profile capable of blending with the needle tip profile, wherein the periphery of the plunger (5) defines a channel (6) in the elongated part (4), and a chamber (7) capable of holding an implant (8), characterized in that the chamber (7) is positioned radially outside the channel (6) and has a directly or indirectly open connection to the channel (6), the plunger (5) being capable of closing off and opening up the chamber (7) by being displaced.

3. An implantation device according to claim 1 or 2, characterized by being loaded with an implant (8) held in the chamber (7).

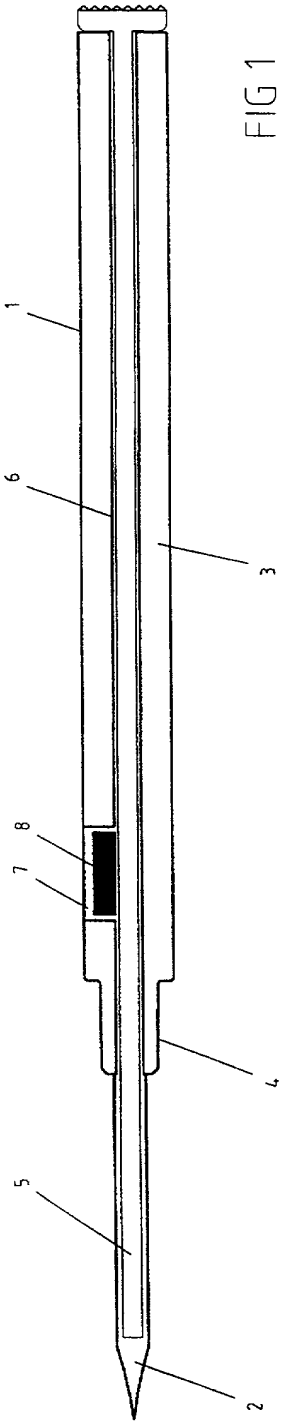

FIG 1

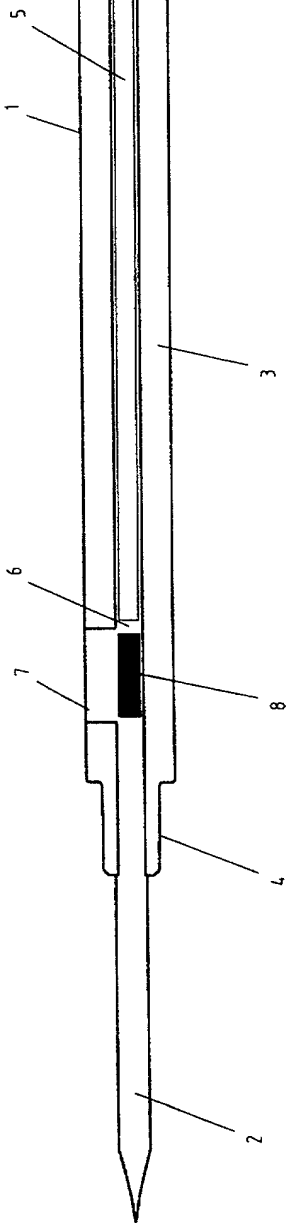

FIG 2

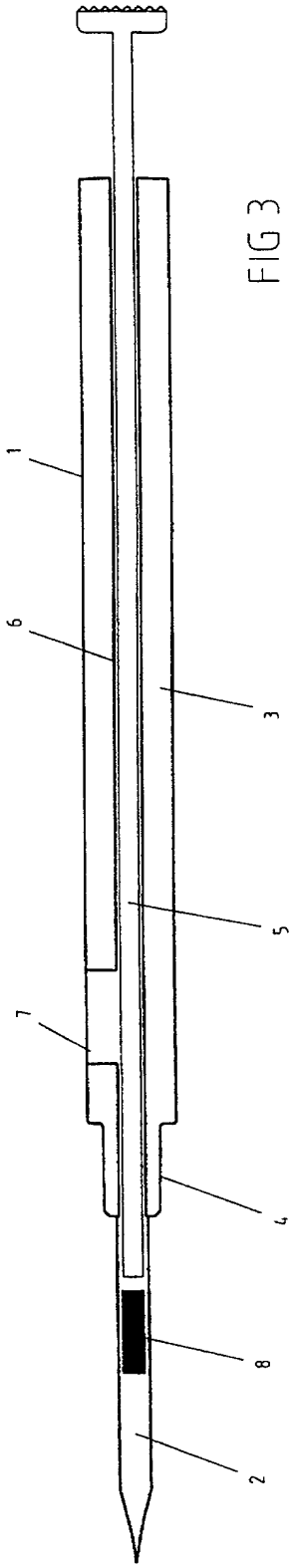

FIG 3

01/97286 US

DECLARATION AND POWER OF ATTORNEY FOR PATENT APPLICATION

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original first and joint inventor (if plural names are listed below) of the subject matter for which a patent is sought on the invention entitled:

"PRELOADED IMPLANTATION DEVICE"

the specification of which
[CHECK ONE]

[ ]is attached hereto

[ ] was filed on _____ as Application Serial No. _____ and was amended on _____ [if applicable]

[x]as filed under the Patent Cooperation Treaty on **June 16, 1998** Serial **PCT/EP98/03712**, The United States of America being designated.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claim(s), as amended by any amendment referred to above.

I acknowledge the duty to disclose to the Patent and Trademark Office all information known to me to be material to patentability as defined Title 37, Code of Federal Regulations Section 1.56(a)

I hereby claim foreign priority benefits under Title 35, United States Code, Section 119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign applications(s) for patent or inventor's certificate having a filing date before that of the application(s) on which priority is claimed:

Prior Foreign Application(s)			Priority claimed
97201891.5	***EP***	***20 / 06 / 1997***	**X** Yes ____ No
Number	Country	Day/Month/Year filed	
_____	_____	___/___/_____	____ Yes ____ No
Number	Country	Day/Month/Year filed	
_____	_____	___/___/_____	____ Yes ____ No
Number	Country	Day/Month/Year filed	

I hereby claim the benefit under Title 35, United States Code, Section 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application(s) in the manner provided by the first paragraph of Title 35, United States Code, Section 112, I acknowledge the duty to disclose to the patent and Trademark
Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56(a) which became available between the filing date of the prior application(s) and the national or PCT international filing date of this application.

(U.S. Serial No.) (Filing date) (Status-patented, pending, abandoned)

(U.S. Serial No. (Filing date) (Status-patented, pending, abandoned)

And I hereby appoint as principal attorney, William M. Blackstone, Registration No. 29,772, Mary E. Gormley, Registration No. 34,409, (3) Gregory R. Muir, Registration No. 35,293 and Michael G. Sullivan, Registration No. 35,377.

Please address all communications to:

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1300 Piccard Drive #206
Rockville, MD 20850-4373

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued theron.

Full name of sole or first inventor *Pieter de HAAN*

Inventor' signature _____ 2 December 1999 Date

Citizenship *Dutch*

Residence and P.O. Address *Amsteleindstraat 32, 5345 AW OSS - The Netherlands* NLX

Full name of second joint inventor *Thomas Jacob BOS* 2 dec 1999

Inventor's signature _____ 2 December 1999 Date

Citizenship *Dutch*

Residence and P.O.Address *Prof. Oudstraat 13, 5344 JR OSS - The Netherlands* NLX

Full name of third joint inventor _____

Inventor's signature _____ Date

Citizenship _____

Residence and P.O.Address _____

Full name of forth joint inventor _____

Inventor's signature _____ Date

Citizenship _____

Residence and P.O.Address _____